Restless Legs Syndrome in an Appalachian Primary Care Population: Prevalence, Demographic and Lifestyle Correlates, and Burden

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Background: Restless legs syndrome (RLS) is a common and distressing sensorimotor disorder of unknown etiology. While the epidemiology of RLS has been examined in several North American and European studies, research on RLS and RLS burden in poor, rural populations, including those residing in Appalachia, remains sparse. In this study, we investigated RLS prevalence in an Appalachian primary care population and examined the association of RLS to demographic factors, lifestyle characteristics, sleep quality, and mood disorders.

Methods: Participants of this anonymous survey study were community-dwelling adults aged ≥ 18 years visiting one of 4 West Virginia primary care clinics. Data gathered included detailed information on sleep patterns, demographic characteristics, lifestyle factors, and health/medical history; the survey also included questions specific to RLS diagnosis and severity. Response rates were excellent, with 68% of eligible adults contacted returning completed surveys ($N = 1,424/2,087$). Pregnant women ($N = 65$) and those with missing data on key variables ($N = 142$) were excluded from the analyses.

Results: Of the 1,217 participants included in the final analytic sample, 19.6% (18.2% with symptoms at least once/month) met the 4 IRLSSG diagnostic criteria in the absence of positional discomfort or leg cramps; 14.5% reported RLS symptoms at least once/week and 10.1% indicated symptoms $\geq 3\times/\text{week}$. Excluding respondents with diabetes, kidney disease, or anemia

reduced these rates only slightly. Those with RLS were more likely to be older, female, lower income, unemployed, disabled, non-Hispanic white, and less likely to be college educated than those without RLS. Mood and sleep impairment were significantly elevated in those with RLS; after adjustment for demographic and lifestyle characteristics, health history, and other factors, those with RLS remained significantly more likely to indicate a history of depression (adjusted odds ratio [OR] = 1.9; 95% confidence interval [CI] = 1.4, 2.6) and anxiety (OR = 1.6, CI 1.1, 2.2), to report sleep impairment both 4 (OR = 2.4, CI 1.6, 3.7) and 7 days/week (OR = 1.8, CI 1.3, 2.4), and a mean sleep duration < 5 h/night (OR = 1.7, CI 1.2, 2.3). These associations increased in both strength and magnitude with increasing symptom frequency (p 's for trend ≤ 0.01).

Conclusions: Findings of this preliminary anonymous survey study suggest that RLS prevalence is high in this Appalachian primary care population and that RLS is associated with significant burden in terms of both mood and sleep impairment.

Keywords: Restless legs syndrome, sleep, mood, depression, anxiety, demographics, socioeconomic status, lifestyle, race, employment

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BRIEF SUMMARY

Current Knowledge/Study Rationale: Restless legs syndrome (RLS) is a common and distressing sensorimotor disorder of unknown etiology. While the epidemiology of RLS has been examined in several North American and European studies, research on RLS and RLS burden in poor, rural populations, including those residing in Appalachia, remains sparse.

Study Impact: Findings of this survey study suggest that RLS prevalence is high in this Appalachian primary care population and that RLS is associated with significant burden in terms of both mood and sleep impairment, and may help explain the elevated rates of depression and sleep deficits reported in WV residents. Larger prospective studies are needed to investigate potential causal relationships and to enhance our still incomplete understanding regarding both the etiology and sequelae of RLS in this and other populations.

sleep impairment,^{8,10,11} the most common presenting complaint of patients seeking medical care for RLS.^{12,13} Likewise, mood

RLS is a burdensome sleep disorder affecting an estimated average of 15% to 20% of the US general adult population.^{1,2} Recognition of RLS as an important clinical condition is growing, in part aided by standardized diagnostic criteria developed by international expert consensus in 1995³ and revised in 2002.⁴ RLS is characterized by a compelling urge to move the legs that is usually accompanied by uncomfortable, often painful sensations in the legs, begins or worsens during periods of inactivity, is worse during the evening and nighttime hours, and is partially or totally relieved by movement.⁴ RLS can have profound negative effects on daily functioning and quality of life (QOL), as well as health care costs and productivity, comparable to those reported in other serious disorders such as Parkinson disease, diabetes, and stroke.⁵⁻⁹ Primary contributing factors to the significant reductions in QOL with RLS are sleep and mood disturbances. RLS is associated with significant

Figure 1—Study flow diagram

disturbance appears common in those affected by RLS,^{10,14} and can both result from and contribute to sleep deficits.¹⁵ RLS has also been linked to increased risk for cardiovascular disease (CVD) and stroke, and has been associated with diabetes and other related chronic conditions.² However, the etiology of RLS remains poorly understood,¹⁶⁻¹⁸ and there is still no cure for RLS.

Prevalence estimates of RLS have varied widely (from 4% to 29%) depending on the study population characteristics, study location, and RLS definition and ascertainment¹; even among the five studies in US primary care populations, prevalence estimates have ranged from 13.3%¹² to 29.3%.¹⁹ Findings have likewise been inconsistent regarding the association of RLS to specific socioeconomic (SES)^{1,6,20-23} and lifestyle characteristics.^{1,6,20-22,24} Moreover, few studies have investigated RLS and RLS burden in poor, rural populations, including those residing in Appalachia. Situated entirely within the Appalachian region, West Virginia is characterized by a rural and socioeconomically disadvantaged population with a health status of citizens among the worst in the country. West Virginia residents rank among the poorest and least educated in the US, and suffer among the highest rates of many

chronic health conditions linked to RLS, including arthritis, obesity, and diabetes.^{2,25-27} Recent CDC analyses of 2006 and 2008 data from the Behavioral Risk Factor Surveillance System (BRFSS) also indicate that West Virginia residents suffer the highest prevalence of both depression²⁸ and insufficient rest or sleep²⁹ in the nation. While RLS prevalence in WV adults is likely high and may help explain the elevated rates of both sleep disturbance and depressive disorders in the state, the prevalence and correlates of RLS in WV residents remain unknown. In this anonymous survey study, we investigated RLS prevalence in a sample of WV primary care patients, and examined the association of RLS to demographic factors, lifestyle characteristics, sleep quality, and mood disorders in this population.

METHODS

Study Population and Survey Administration

Participants for this study were ambulatory, community-dwelling, English-speaking adults ≥ 18 years of age visiting 1 of 4 Morgantown area primary care clinics affiliated with the West Virginia University (WVU) Health Sciences Center, and residing in the Morgantown area. Following a brief description of the study, surveys were offered to each patient in the clinic waiting area; eligible participants interested in participating in the study were asked to place the completed survey in an onsite, clearly labeled drop box. Research staff provided assistance to those who wished to participate but were unable to read due to illiteracy or visual impairment. The survey was presented to potential participants as a study regarding sleep patterns in all Morgantown area adults, including both those who slept well and those who did not. Surveys were distributed during 3- to 4-hour time blocks (between the hours of 8 AM and 5:30 PM, Monday-Friday), over the course of 12 weeks; survey administration times and days of the week were rotated systematically in each clinic to ensure similar coverage across clinics and to reduce the probability of selection bias based on timing of survey administration. The survey instrument included 41 self-report items and required 5-10 minutes to complete. Survey responses were anonymous, and no personally identifying information was collected. Data gathered included detailed information on: sleep duration and quality during the past 7 days; demographic characteristics; lifestyle; current height and weight; history of physician diagnosed chronic health conditions, including depression and anxiety; current medications for these conditions; and, in women, reproductive history. This anonymous survey study was approved by the West Virginia University Institutional Review Board.

As illustrated in **Figure 1**, a total of 2,392 patients were approached regarding participation in the study. Of these, 305 were ineligible to participate (due to age under 18, residence out of the catchment area, inability to understand English, or other factors). Of the remaining 2,087 adults contacted, 1,538 patients indicated interest in participating and accepted the survey. Of these 1,538 surveys distributed, 1,424 completed surveys were collected from the drop boxes, yielding an overall survey response rate of 68%. Representation was approximately equal among the 4 clinics (N = 352, 353, 355, and 364), although response rates varied slightly from 66% to 77%. Women were more likely to respond than men (76.7% vs. 65.4%, respectively,

$p = 0.0004$). Pregnant women ($N = 65$) were excluded from the analytic sample, leaving a total of 1,359 eligible adults. Exclusion of those with any missing data on RLS symptoms ($N = 27$, 2.0%) and on demographics, lifestyle characteristics, sleep profiles, and other covariates of interest ($N = 115$, 8.1%), yielded a final analytic sample of 1,217 primary care patients. Those with missing data were more likely to be older (52.2 ± 0.5 vs. 47.2 ± 2.0 years, $p = 0.005$) and retired (33% vs. 18%, $p = 0.02$), and were less likely to be college graduates (18% vs. 34%, $p = 0.001$), be physically active (38 vs. 52%, $p = 0.02$), and report an annual income over \$25,000 (50% vs. 72%, $p < 0.001$) than those without missing data. Relative to those included in the analysis, participants with incomplete data did not differ in other demographic or lifestyle characteristics, or in sleep patterns, health profiles, or other factors ($p > 0.2$).

Measurement of Outcomes, Indices of Burden, and Major Covariates

Ascertainment of RLS

The primary outcome of interest, RLS was assessed via responses to 7 survey questions adapted from a previously validated, 7-item self-report diagnostic questionnaire³⁰ and designed to capture the 4 International Restless Legs Syndrome Study Group's (IRLSSG) diagnostic criteria (**Figure 2**),⁴ exclude common RLS mimics (leg cramps and positional discomfort), and determine presence of accompanying unpleasant sensations. After a small pilot survey suggesting that certain items in the original validated RLS questionnaire might be confusing to some participants, we adapted the wording of some questions to render them simpler and easier for our target population to understand. To ensure we were indeed capturing the same symptom cluster as the original questionnaire items, we surveyed a sample of 118 non-pregnant adults visiting the 4 target clinics using the original 7 questionnaire items³⁰. This survey produced broadly comparable results in terms of prevalence, correlates, and associated burden as did our revised survey, yielding an overall prevalence rate of 18.1%, with 16.7% of participants reporting symptoms $\geq$ once/month, and 11.1% reporting symptoms $\geq 3\times$ /week. However, as suggested by the confusion expressed by some participants in our pilot survey, the rate of missing data was much higher for the RLS items using the original vs. our revised questionnaire (15.3% vs. 1.9%).

The adapted questionnaire included the following questions: (1) "Do you ever have an urge to move your legs that is difficult to resist?" If YES: (2) Will simply changing leg position by itself once without continuing to move usually relieve these feelings?" (3) "Is this urge to move usually accompanied by unpleasant sensations in the legs?" (4) "Are the unpleasant sensations due to leg cramping?" (5) "Does the urge to move or unpleasant sensations begin or worsen during periods of rest or inactivity such as lying or sitting?" (6) "Is the urge to move or the unpleasant sensations partially or totally relieved by movement, such as walking or stretching?"; and (7) "Does the urge to move or the unpleasant sensations only occur or get worse in the evening or night?" RLS symptom frequency was ascertained via an 8th question: "How often do you experience these symptoms?" (Circle one: less than once/month, 1-3 days/month, 1-2 days/week, and 3 or more days/week). RLS was defined as an affirmative response to all 4 RLS

Figure 2—Diagnostic criteria for restless legs syndrome

IRLSSG Essential Criteria (2003)⁴

- (1) An urge to move the legs, usually accompanied or caused by uncomfortable and unpleasant sensations in the legs (Sometimes the urge to move is present without the uncomfortable sensations and sometimes the arms or other body parts are involved in addition to the legs);
- (2) The urge to move or unpleasant sensations begin or worsen during periods of rest or inactivity such as lying or sitting;
- (3) The urge to move or unpleasant sensations are partially or totally relieved by movement, such as walking or stretching, at least as long as the activity continues;
- (4) The urge to move or unpleasant sensations are worse in the evening or night than during the day or only occur in the evening or night. (When symptoms are very severe, the worsening at night may not be noticeable but must have been previously present.)

diagnostic questions (#1, 5-7, above) and a negative response to questions 2 and 4. Since the presence of unpleasant sensations is not an essential diagnostic criterion for RLS, but rather an often associated characteristic,⁴ the prevalence and correlates of RLS with unpleasant sensations were assessed in separate analyses. Participants were also asked, in a separate section of the questionnaire, if they had received a physician diagnosis of RLS and/or were taking medications for RLS.

Demographic and Lifestyle Characteristics

Demographic characteristics were assessed via self-report survey questions, and included age, gender, race/ethnicity, education (< 12 years, high school graduate, some college, ≥ 4 years post high school [college graduate]), employment status (employed, unemployed/out of work, homemaker, retired, student, disabled), marital status (single, married or cohabiting, widowed, divorced), annual household income ($< \$25,000$, $\$25,000$ - $50,000$, $\$50$ - $75,000$, $> \$75,000$). Lifestyle factors assessed included caffeine consumption (2 items), smoking history and current status (5 items), and engagement in physical activity (2 items).

Sleep and Mood Disturbance

Five survey items assessed number of days (0-7) during the past week that the participant experienced specific sleep problems (early awakening, difficulty falling asleep, difficulty staying asleep, daytime fatigue/somnolence, and insufficient rest). An additional, open-ended question was used to ascertain sleep duration (in hours and minutes) during the past week. The items were adapted from a series of questions regarding sleep quality and duration introduced to the National Health and Nutrition Examination Survey (NHANES) in the 2005-6 cycle.³¹ Participants were considered to have a history of a specific mood disorder, including depression and anxiety, if they reported receiving a physician diagnosis of the condition and/or indicated they were currently taking prescription medications for this disorder in response to specific structured queries.

Other Health-Related Factors

BMI was calculated as (weight in kg/height in m^2). Obesity was defined as BMI ≥ 30 . History of a specific chronic health

disorder (anemia, hypertension, high cholesterol, heart disease, stroke, kidney disease, diabetes, osteoarthritis, rheumatoid arthritis, and other conditions) was defined as reported physician diagnosis of, and/or currently taking prescription medications for, this disorder.

Analysis

All data were analyzed using SPSS v. 20. Prevalence estimates for RLS were adjusted for age and sex using WV 2010 census data³² and calculated both overall and by symptom frequency (any frequency, at least once/week, and $\geq 3\times/\text{week}$). Potential differences between participants with and without missing data were evaluated using the Student *t*-test or Mann-Whitney U Test for continuous or ordinal variables, and χ^2 test for categorical variables. We used multiple logistic regression to determine the independent associations of RLS to demographic and lifestyle factors, depression, anxiety, and sleep disturbances, and to assess the influence of potential confounders and effect modifiers; linear trends were assessed using polynomial contrasts. Unless stated otherwise, multivariable models were adjusted for demographic factors and lifestyle characteristics, as well as BMI and comorbid conditions, including anemia, kidney disease, heart conditions, hypertension, and diabetes. All *p*-values presented are 2-sided.

Sleep duration was assessed as both a dichotomous (< 5 h vs. ≥ 5 h/night) and a continuous variable. Similarly, we analyzed sleep quality as both a dichotomous variable (reported sleep problems 4 and 7 days/week) and a continuous variable (total and mean score of the 5 sleep quality questions). Component questions were analyzed both individually and as a composite score. Scale reliability testing of completed questionnaires indicated adequate internal consistency of the grouped 5 items (Cronbach $\alpha = 0.85$). To determine the utility of the 5-item scale, we also ran a Principal Components factor analysis, using an eigenvalue cutoff value of 1.5 and factor loading of 0.65. All items loaded strongly on one domain (loading values 0.77-0.83, eigenvalue = 3.2) and explained 63% of the total variance, with the Kaiser-Meyer-Olkin (KMO) measure of sampling adequacy (0.81) and Bartlett test values ($p < 0.0001$) further supporting use of the composite scale.

RESULTS

Table 1 gives the crude and age- and sex-adjusted prevalence rates for RLS for the entire population, the analytic sample, and a population subset that excludes participants with specific conditions linked to RLS. Of the 1,217 respondents included in this analysis, 19.6% (17.9% adjusted for age and sex) met the 4 IRLSSG diagnostic criteria and/or reported a physician diagnosis of RLS and did not report symptoms due to leg cramps or positional discomfort; of the 238 respondents with RLS, 93% (18.2% of total respondents) indicated symptoms at least once/month (**Table 1**). Over 70% of those meeting criteria for RLS (14.5% of total respondents) reported symptoms at least once/week, and $> 50\%$ (10.1% of total respondents) indicated symptoms $\geq 3\times/\text{week}$. Restricting RLS cases to those whose symptoms were accompanied by unpleasant sensations slightly reduced prevalence estimates (16.8% for any frequency symptoms, 15.6% for symptoms $\geq$ once/month,

12.4% for symptoms $\geq$ once/week, 9.0% for symptoms $\geq 3\times/\text{week}$). Excluding respondents with diabetes, kidney disease, or anemia attenuated the overall prevalence rates only slightly (RLS prevalence rates = 18.1% for any frequency symptoms (17.5% adjusted for age and sex), 16.9% for symptoms $\geq$ once/month (17.0% adjusted), 13.2% for symptoms $\geq$ once/week (13.2% adjusted), and 8.4% for symptoms $\geq 3\times/\text{week}$ (8.9% adjusted) (**Table 1**). Likewise, excluding those on medications for depression or anxiety resulted in only a modest reduction in overall prevalence estimates (17.7% for any frequency symptoms, 16.3% for symptoms $\geq$ once/month, 12.6% for symptoms $\geq$ once/week, and 8.6% for symptoms $\geq 3\times/\text{week}$ [data not shown]). Thirteen respondents reported a diagnosis of RLS but did not meet current RLS symptom criteria.

Of the 238 participants in our analytic sample meeting all criteria for RLS, only 66 (28%) had received a physician diagnosis, of whom 31 (13% of those meeting criteria for RLS) were on RLS medications. Interestingly, of the 66 respondents who were diagnosed with RLS, those currently on RLS medications were over $3\times$ more likely than those who were not on medication to report symptoms $\geq 3\times/\text{week}$ (OR adjusted for age and sex = 3.1, CI 1.0, 9.7).

Study population characteristics by RLS status are given in **Table 2**. Participants were predominantly female (64%), non-Hispanic white (92%), over 40 years of age (65%), and married or cohabiting (68%). Fewer than 35% had completed at least 4 years of college, and approximately 50% reported an annual household income of under \$50,000. Almost 40% of participants were obese, and $> 60\%$ reported at least one comorbid health condition, with 24% reporting ≥ 3 comorbid disorders.

Association of RLS to Demographic, Lifestyle, and Health Characteristics

Participants with RLS were significantly more likely to be older, non-Hispanic white, female, and unemployed or disabled and less likely to be college-educated or to report a family income over \$75,000 after adjustment for other demographic, lifestyle, and health-related factors (**Table 2**). RLS was also significantly and positively related to obesity (OR = 1.5, 95% CI 1.1, 2.0) and to comorbidity, with likelihood of RLS increasing with increasing number of comorbid conditions. Those with RLS also appeared less likely to be from minority populations (OR = 0.6, CI 0.3, 1.0). While RLS was significantly related to sedentary lifestyle and current smoking in the unadjusted analysis (OR for exercise < 1 h/week = 1.4, CI 1.0, 1.9; OR for current smoking = 1.5, CI 1.0, 2.1), adjustment for other factors attenuated these associations (OR's = 1.2 [0.8, 1.6] and 1.3 [0.9, 1.9], respectively). RLS did not appear related to marital status or to caffeine consumption in this population. Restriction of RLS cases to those reporting symptoms $\geq 1-2\times/\text{week}$ slightly strengthened the protective association between RLS and minority status (adjusted OR = 0.30, CI 0.1, 0.8) and college education (adjusted OR = 0.4, 0.2, 0.7), but did not alter the association of other demographic or lifestyle factors to RLS.

Association of RLS to Mood and Sleep Disturbance

RLS was associated with significantly increased sleep and mood disturbance in this population (**Table 3**). Those with RLS

Table 1—Restless legs syndrome (RLS) prevalence* in an adult West Virginia primary care population

	RLS prevalence (%)			
	All participants		Excluding those with missing data	
	Crude	Age and sex-adjusted**	Crude	Age and sex-adjusted**
Total population	N = 1,398		N = 1,280	
Any frequency RLS symptoms	19.96	17.90	19.45	17.77
RLS symptoms at least once/month	18.81	17.42	18.20	17.15
RLS symptoms at least once/week	14.88	13.68	14.53	13.71
RLS symptoms at least 3×/week	10.37	9.98	10.16	9.85
RLS symptoms with unpleasant sensations	17.17	15.34	16.72	15.10
Sx at least once/month	16.17	15.11	15.63	14.90
Sx at least once/week	12.88	11.65	12.42	11.55
Sx at least 3×/week	9.23	8.90	8.98	8.77
Excluding pregnant women	N = 1,334		N = 1,217†	
Any frequency RLS symptoms	19.63	17.94	19.56	17.94
RLS symptoms at least once/month	18.53	17.39	18.24	17.11
RLS symptoms at least once/week	14.63	13.60	14.54	13.59
RLS symptoms at least 3×/week	10.15	9.87	10.11	9.72
RLS symptoms with unpleasant sensations	16.91	15.53	16.76	15.29
Sx at least once/month	15.88	15.12	15.61	14.82
Sx at least once/week	12.65	11.65	12.41	11.52
Sx at least 3×/week	9.04	8.89	8.96	8.68
Excluding pregnant women and participants with a physician diagnosis of diabetes, kidney disease, or anemia	N = 1,024		N = 926	
Any frequency RLS symptoms	18.13	17.74	18.10	17.52
RLS symptoms at least once/month	17.07	17.30	16.90	17.04
RLS symptoms at least once/week	13.21	13.39	13.20	13.21
RLS symptoms at least 3×/week	8.87	9.30	8.40	8.85
RLS symptoms with unpleasant sensations	15.33	14.84	15.27	14.65
Sx at least once/month	14.37	14.56	14.18	14.59
Sx at least once/week	11.19	11.10	11.01	10.97
Sx at least 3×/week	7.91	8.18	7.42	7.88

*RLS defined as meeting all 4 IRLSSG criteria in the absence of leg cramps or positional discomfort.⁵⁶ **Adjusted prevalence estimates calculated using Monongalia County, WV 2010 census data.³² †Analytic sample for the present study. Sx, symptoms.

were approximately twice as likely to report a history of depression (OR adjusted for demographic characteristics = 1.9, CI 1.4, 2.6) or anxiety disorders (adjusted OR = 1.6 [1.1, 2.2]) and to be taking medications for these conditions (adjusted ORs = 1.5 [CI 1.1, 2.2] and 1.6 [CI 1.1, 2.3, respectively]). Similarly, those meeting criteria for RLS were over twice as likely to report symptoms of sleep disturbance ≥ 4 days/week after adjustment for demographic and other factors, including difficulty falling asleep (OR = 2.1, CI 1.6, 2.9), difficulty staying asleep (OR = 2.3, CI 1.8, 3.2), awakening too early (OR = 2.3, CI 1.7, 3.0), feeling sleepy or tired during the day (OR = 2.4, CI 1.7, 3.5), or receiving insufficient rest (OR = 2.5, CI 1.8, 3.4) (Table 3). Likewise, those with RLS were approximately twice as likely to suffer daily sleep disturbance symptoms (adjusted ORs = 1.7 to 1.9) as those not meeting criteria for RLS (Table 3). Reported sleep duration was strongly and inversely associated with RLS (OR per 30-min increment = 0.8, CI 0.7, 0.9), with participants meeting RLS criteria 70% more likely to report sleeping < 5 h/night (OR = 1.7, CI 1.2, 2.3). Again, of

the 66 participants who had received an RLS diagnosis, those who were on RLS medications appeared over twice as likely to indicate a history of depression or anxiety (OR adjusted for age and sex = 2.3, CI = 0.9, 6.0), and were approximately 3× as likely to be currently taking medications for these conditions (adjusted OR = 3.2, CI 1.1, 8.9), and to report insufficient rest daily (adjusted OR = 2.6, CI 1.0, 7.3) relative to those not on RLS medication.

As illustrated in Table 4, the associations of RLS to sleep and mood disturbance increased progressively in both strength and magnitude with rising symptom frequency. For example, compared to those without RLS, the relative odds of reporting a diagnosis of depression showed a significant, progressive increase from 1.5 (CI 0.85, 2.6) in those reporting symptoms less than once per week to 2.5 (CI 1.7, 3.7) in those with symptoms $\geq 3\times/\text{week}$ (p 's for trend ≤ 0.0001). Similarly, the likelihood of diagnosed anxiety disorder increased progressively with increasing RLS symptom frequency (OR's for symptoms $< 1\times/\text{week}$, $1-2\times/\text{week}$, and $\geq 3\times/\text{week}$ = 1.1 (0.7, 1.9), 2.0 (1.1, 3.6),

Table 2—Demographic and lifestyle characteristics of non-pregnant adults ≥ 18 years of age attending 4 primary care clinics, stratified by RLS (N = 1,217)

	Total (N = 1,217)		No RLS (N = 979)		RLS (N = 238)		Crude OR (95% CI)	p*	Adjusted OR** (95% CI)	p*
	N	%	N	%	N	%				
Demographic Characteristics										
Age (years)								0.04		0.04
18-40	444	36.48	376	38.41	68	28.57	1.00 (Referent)		1.00 (Referent)	
41-50	238	19.56	187	19.10	51	21.43	1.51 (1.01,2.26)	0.05	1.61 (1.05,2.47)	0.05
51-60	239	19.64	182	18.59	57	23.95	1.73 (1.17,2.57)	0.006	1.83 (1.20,2.79)	0.005
61-70	187	15.37	149	15.22	38	15.97	1.41 (0.96,2.19)	0.09	1.38 (0.87,2.20)	0.17
≥ 71	109	8.96	85	8.68	24	10.08	1.56 (1.00,2.63)	0.05	1.75 (1.00,3.05)	0.05
Test for trend								0.04		0.04
Per year increment							1.01 (1.00,1.02)	0.05	1.01(1.00,1.02)	0.04
Mean age in years (SE)	47.33 (0.48)		46.94 (0.53)		48.93 (1.07)			0.05		
Gender								0.01		0.01
Male	440	36.15	371	37.90	69	28.99	1.00 (Referent)		1.00 (Referent)	
Female	777	63.85	608	62.10	169	71.01	1.50 (1.10, 2.04)		1.52 (1.10,2.10)	
Race/Ethnicity								0.02		0.01
Non-Hispanic White	1,118	91.87	890	90.91	228	95.80	1.00 (Referent)		1.00 (Referent)	
Minority	99	8.13	89	9.09	10	4.20	0.44 (0.23,0.86)		0.43 (0.22,0.84)	
Marital status								0.73		0.57
Married/co-habiting	829	68.12	669	68.34	160	67.23	1.00 (Referent)		1.00 (Referent)	
Widowed/separated/divorced	225	18.49	177	18.08	48	20.17	1.14 (0.79,1.63)	0.50	1.08 (0.66,1.77)	0.72
Single, never married	163	13.39	133	13.59	30	12.61	0.94 (0.61,1.45)	0.79	0.72 (0.47,1.09)	0.12
Years of education								0.001		0.02
< 12 years	81	6.66	61	6.23	20	8.40	1.00 (Referent)		1.00 (Referent)	
High school/GED	328	26.95	248	25.33	80	33.61	0.98 (0.56,1.73)	0.95	0.94 (0.52,1.70)	0.76
Some college/technical school	384	31.55	302	30.85	82	34.45	0.83 (0.47,1.45)	0.51	0.81 (0.45,1.47)	0.49
4+ years college	424	34.84	368	37.59	56	23.53	0.46 (0.26,0.83)	0.009	0.52 (0.28,0.98)	0.04
Current employment status								0.002		0.08
Employed/student	699	57.44	585	59.75	114	47.90	1.00 (Referent)		1.00 (Referent)	
Homemaker	102	8.38	82	8.38	20	8.40	1.25 (0.74,2.12)	0.41	1.12 (0.63,1.98)	0.69
Retired	221	18.16	175	17.88	46	19.33	1.35 (0.92,1.98)	0.12	1.12 (0.67,1.86)	0.66
Unemployed/laid off	70	5.75	50	5.11	20	8.40	2.05(1.17,3.58)	0.01	2.01 (1.09,3.70)	0.025
Disabled	125	10.27	87	8.89	38	15.97	2.24 (1.46,3.45)	0.0002	1.73 (1.05,2.84)	0.03
Average Household Income										
< \$25, 000	311	25.55	232	23.70	79	33.19	1.00 (Referent)		1.00 (Referent)	
\$25,000-\$49,999	303	24.90	243	24.82	60	25.21	0.73 (0.50,1.06)	0.10	0.81 (0.54,1.21)	0.30
\$50,000-\$74,999	233	19.15	185	18.90	48	20.17	0.76 (0.51,1.15)	0.19	0.93 (0.60,1.44)	0.75
≥ \$75,000	277	22.76	239	24.41	38	15.97	0.47 (0.31,0.72)	0.0005	0.63 (0.40,1.00)	0.05
Don't know	93	7.64	80	8.17	13	5.46	0.48 (0.25,0.91)	0.02	0.46 (0.24,1.08)	0.09
P for trend								0.006		0.05
Lifestyle Characteristics										
Smoking status								0.09		0.37
Never	577	47.41	476	48.62	101	42.44	1.00 (Referent)		1.00 (Referent)	
Former	355	29.17	284	29.01	71	29.83	1.18 (0.84, 1.65)	0.34	1.13 (0.80,1.61)	0.45
Current	277	22.76	211	21.55	66	27.73	1.47 (1.04,2.09)	0.03	1.29 (0.87,1.92)	0.21
Unsure	8	0.66	8	0.82	0	0.00	0.35 (0.11,3.46)	0.35	0.82 (0.45,2.75)	0.65
Exercise at least one hour/week								0.07		0.38
Yes	528	43.39	438	44.74	90	37.82	1.00 (Referent)		1.00 (Referent)	
No	473	38.87	370	37.79	103	43.28	1.38 (1.01,1.89)	0.04	1.20 (0.81, 1.58)	0.16
Unsure	216	17.75	171	17.47	45	18.91	1.28 (0.86,1.91)	0.22	1.13 (0.78,1.84)	0.41
Drink at least 5 8 oz caffeinated beverages/week								0.71		0.69
No	289	23.75	235	24.00	54	22.69	1.00 (Referent)		1.00 (Referent)	
Yes	924	75.92	742	75.79	182	76.47	1.07 (0.77,1.49)	0.67	0.96 (0.67,1.38)	0.81
Unsure	4	0.33	2	0.20	2	0.84	0.96 (0.55,1.92)	0.81	0.98 (0.44, 1.98)	0.77
Comorbidity										
Comorbid condition(s)t								0.00003		0.001
No	476	39.11	411	41.98	65	27.31	1.00 (Referent)		1.00 (Referent)	
Yes	741	60.89	568	58.02	173	72.69	1.93 (1.41,2.61)		1.82 (1.26,2.64)	
Number of comorbid conditions								0.0002		0.006
None	476	39.11	411	41.98	65	27.31	1.00 (Referent)		1.00 (Referent)	
One	259	21.28	207	21.14	52	21.85	1.59 (1.06,2.37)	0.02	1.56 (1.01,2.40)	0.04
Two	189	15.53	144	14.71	45	18.91	1.98 (1.29,3.02)	0.002	2.01(1.24,3.25)	0.005
Three or more	293	24.08	217	22.17	76	31.93	2.22 (1.53,3.21)	0.00002	2.17(1.37,3.44)	0.001
P for trend								0.0002		0.006

*All p-values are 2-sided. **Adjusted for other sociodemographic factors in table. CI, confidence intervals; OR, odds ratio; SE, standard error. †, Reported physician diagnosis of anemia, hypertension, high cholesterol, heart disease, stroke, kidney disease, diabetes, osteoarthritis, rheumatoid arthritis, lung disease, or other serious chronic conditions.

Table 3—Association of RLS to sleep and mood disturbance in non-pregnant adults ≥ 18 years of age attending 4 WVU primary care clinics

			Total (N = 1,217)		No RLS (N = 979)		RLS (N = 238)		Adjusted OR (95% CI) [†]	p ^{*,†}
			N	%	N	%	N	%		
Mood Disturbance										
Depression										
History of depression*	No		898	73.79	751	76.71	147	61.76	1.00 (Referent)	0.00006
	Yes		319	26.21	228	23.29	91	38.24	1.88 (1.39,2.56)	
On medications for depression	No		991	81.43	815	83.25	176	73.95	1.00 (Referent)	0.015
	Yes		226	18.57	164	16.75	62	26.05	1.53 (1.09,2.15)	
Anxiety										
History of anxiety disorder*	No		950	78.06	783	79.98	167	70.17	1.00 (Referent)	0.001
	Yes		267	21.94	196	20.02	71	29.83	1.61 (1.14,2.22)	
On medications for anxiety	No		1,047	86.03	855	87.33	192	80.67	1.00 (Referent)	0.02
	Yes		170	13.97	124	12.67	46	19.33	1.55 (1.08,2.29)	
History of depression or anxiety	No		815	66.97	681	69.56	134	56.30	1.00 (Referent)	0.001
	Yes		402	33.03	298	30.44	104	43.70	1.65 (1.22,2.28)	
Sleep Disturbance										
Symptom(s) ≥ 4 days/week										
Any symptom	No		274	22.51	245	25.03	29	12.18	1.00 (Referent)	0.00005
	Yes		943	77.49	734	74.97	209	87.82	2.42 (1.58,3.71)	
Difficulty falling asleep	No		766	62.94	654	66.80	112	47.06	1.00 (Referent)	< 0.00001
	Yes		451	37.06	325	33.20	126	52.94	2.11 (1.56,2.86)	
Difficulty staying asleep	No		645	53.00	562	57.41	83	34.87	1.00 (Referent)	< 0.00001
	Yes		572	47.00	417	42.59	155	65.13	2.33 (1.75,3.15)	
Waking too early	No		669	54.97	578	59.04	91	38.24	1.00 (Referent)	< 0.00001
	Yes		548	45.03	401	40.96	147	61.76	2.25 (1.67,3.04)	
Feel sleepy or tired during day	No		441	36.24	391	39.94	50	21.01	1.00 (Referent)	< 0.00001
	Yes		776	63.76	588	60.06	188	78.99	2.43(1.72,3.45)	
Insufficient rest	No		536	44.04	469	47.91	67	28.15	1.00 (Referent)	< 0.00001
	Yes		681	55.96	510	52.09	171	71.85	2.48(1.79,3.43)	
Symptom(s) 7 days/week										
Any symptom	No		615	50.53	523	53.42	92	38.66	1.00 (Referent)	0.0002
	Yes		602	49.47	456	46.58	146	61.34	1.80 (1.32,2.40)	
Difficulty falling asleep	No		1,012	83.16	836	85.39	176	73.95	1.00 (Referent)	0.0004
	Yes		205	16.84	143	14.61	62	26.05	1.90 (1.34,2.70)	
Difficulty staying asleep	No		934	76.75	772	78.86	162	68.07	1.00 (Referent)	0.002
	Yes		283	23.25	207	21.14	76	31.93	1.70 (1.20,2.27)	
Waking too early	No		949	77.98	787	80.39	162	68.07	1.00 (Referent)	0.0001
	Yes		268	22.02	192	19.61	76	31.93	1.91 (1.38,2.64)	
Feel sleepy or tired during day	No		780	64.09	656	67.01	124	52.10	1.00 (Referent)	0.00005
	Yes		437	35.91	323	32.99	114	47.90	1.84 (1.37,2.48)	
Insufficient sleep	No		936	76.91	776	79.26	160	67.23	1.00 (Referent)	0.0001
	Yes		281	23.09	203	20.74	78	32.77	1.86 (1.35,2.56)	
Sleep disturbance in last week, mean days/week (SE) [†]										
Average symptom score			3.60 (0.06)		3.38 (0.06)		4.45 (0.12)		< 0.00001	
Difficulty falling asleep			2.79 (0.08)		2.55 (0.08)		3.76 (0.16)		< 0.00001	
Difficulty staying asleep			3.42 (0.07)		3.17 (0.09)		4.37 (0.16)		< 0.00001	
Waking too early			3.27 (0.08)		3.05 (0.08)		4.10 (0.17)		< 0.00001	
Feel sleepy or tired during day			4.57 (0.07)		4.36 (0.07)		5.38 (0.13)		< 0.00001	
Insufficient sleep			3.96 (0.07)		3.76 (0.07)		4.69 (0.14)		< 0.00001	
Sleep duration (past week)										
Less than 5 hours/night	No		840	69.02	703	71.81	137	57.56	1.00 (Referent)	0.001
	Yes		377	30.98	276	28.19	101	42.44	1.70 (1.24,2.30)	
Per 30 minute increment									0.82 (0.74,0.90)	
Adjusted mean (SE) [†]			6.12 (0.06)		6.24 (0.06)		5.71 (0.10)		< 0.00001	

*All p-values are 2-sided. [†]Adjusted for demographic characteristics (age, sex, race/ethnicity, marital status, education, occupation, and income). CI, confidence intervals; OR, odds ratio; SE, standard error.

Table 4—Association of RLS to sleep and mood disturbance by frequency of RLS symptoms (N = 1,217 adults ≥ 18 years of age attending 1 of 4 WV primary care clinics)

	RLS symptom frequency						p for trend
	< 1×/week (N = 61 cases)		1-2×/week (N = 54 cases)		≥ 3×/week (N = 123 cases)		
	OR (95% CI)**	p*	OR (95% CI)**	p*	OR (95% CI)**	p*	
Mood Disturbance							
Depression							
History of depression	1.50 (0.85,2.59)	0.19	1.85 (1.04,3.29)	0.04	2.47 (1.66,3.66)	< 0.00001	0.00004
On medications for depression	1.14 (0.77,2.08)	0.35	1.65 (0.86,3.07)	0.13	2.10 (1.36,3.21)	0.0007	0.006
Anxiety							
History of anxiety disorder	1.10 (0.67,1.92)	0.54	1.96 (1.08,3.55)	0.03	2.24 (1.34,3.10)	0.0001	0.002
On medications for anxiety	1.05 (0.54,2.16)	0.79	1.36 (0.65,2.85)	0.42	2.29 (1.36,3.42)	0.001	0.01
History of depression or anxiety	1.29 (0.77,2.19)	0.34	1.87 (1.07,3.28)	0.03	2.20 (1.45,3.15)	0.0002	0.00003
Sleep Disturbance							
Symptom(s) ≥ 4 days/week							
Any symptom	1.23 (0.69,2.23)	0.41	2.37 (1.05,5.54)	0.04	4.63 (2.30,9.33)	0.00002	0.00007
Symptom(s) 7 days/week							
Any symptom	1.21 (0.73,2.02)	0.37	1.32 (0.81,2.17)	0.28	2.90 (1.92,4.38)	< 0.00001	< 0.00001
Sleep disturbance in last week, mean days/week (SE)**							
Average symptom score	3.76 (0.23)		4.01 (0.23)		5.03 (0.17)	< 0.00001 (F = 28.07)†	
Difficulty falling asleep	3.00 (0.32)		3.46 (0.34)		4.31 (0.23)	< 0.00001 (F = 19.54)†	
Difficulty staying asleep	3.62 (0.33)		3.97 (0.36)		4.89 (0.24)	< 0.00001 (F = 16.34)†	
Waking too early	3.30 (0.33)		3.67 (0.35)		4.75 (0.21)	< 0.00001 (F = 15.72)†	
Feel sleepy or tired during day	4.82 (0.29)		4.89 (0.30)		5.93 (0.21)	< 0.00001 (F = 17.79)†	
Insufficient sleep	4.09 (0.28)		4.07 (0.31)		5.34 (0.20)	< 0.00001 (F = 17.74)†	
Sleep duration (past week)							
Less than 5 hours/night	1.22 (0.69, 2.15)	0.49	1.63 (0.94,2.93)	0.08	2.55 (1.66,3.60)	< 0.00001	< 0.001
Per 30 minute increment	0.95 (0.81,1.13)	0.59	0.83 (0.68,0.98)	0.03	0.73 (0.64,0.83)	< 0.00001	< 0.001
Mean hours sleep (SE)**	6.12 (0.23)		5.77 (0.25)		5.46 (0.14)	0.00006 (F = 7.47)†	

*All p-values are 2-sided. **Adjusted for age and sex. [†]Univariate ANOVA adjusted for age and sex.

2.2 [1.3, 3.1], respectively; p for trend = 0.002) (**Table 4**). Associations of RLS to current treatment for anxiety and depression showed a similar, strong progressive increase in strength and magnitude with increasing symptom frequency (**Table 4**).

Likewise, the elevated likelihood of sleep disturbance ≥ 4 days a week in those with RLS rose from a modest, nonsignificant 20% in those with symptoms less than once per week (OR = 1.2, CI 0.7, 2.2) to almost 5-fold in those with frequent symptoms (4.6, CI 2.3, 9.3) (p for trend = 0.00007). The relation of RLS to daily sleep disturbance and to reduced sleep duration showed a similar pattern, as did the association of RLS to both composite and individual sleep disturbance scores. Additional adjustment for BMI and comorbidity did not appreciably alter these associations, nor did excluding those with conditions previously linked to RLS, including diabetes, kidney disease, and anemia. Likewise, restricting RLS cases to those with unpleasant leg sensations slightly strengthened, but did not otherwise materially change the associations with sleep impairment (ORs = 2.5 [1.6, 3.8] and 1.9 [1.4, 2.6] for sleep disturbance at least 4 and 7 days/week, respectively), or with depression and anxiety

(ORs = 2.2 [1.6, 3.1] and 1.9 [1.3, 2.6], respectively). Similarly, expanding RLS cases to include the 13 respondents who were diagnosed with RLS but did not meet all questionnaire criteria did not appreciably change any of the associations observed.

DISCUSSION

To our knowledge, this is the first study of RLS to target an Appalachian primary care population. In brief, findings of this survey suggest that prevalence of RLS is high among Morgantown area primary care patients; 19.6% (17.9% adjusted for age and sex) met criteria for RLS, with 14.5% reporting symptoms at least once/week and 10.1% indicating symptoms at least 3×/week. Excluding respondents with diabetes, kidney disease, or anemia reduced these rates only slightly. Fewer than one-third of those meeting RLS criteria had received a physician diagnosis of RLS, and only 13% were on any RLS treatment. Interestingly, of respondents with RLS who reported receiving a physician diagnosis, those who were on medications were more likely to report symptoms at least 3 days/week, as well as depression,

anxiety, and daily sleep disturbance, suggesting that treatment may not have been effective for many of these individuals.

RLS in this population was associated with significant burden. Those meeting criteria for RLS were 50% to 90% more likely to report a history of depression or anxiety disorders and to be taking medications for these conditions; likewise, participants with RLS were over twice as likely to report symptoms of sleep disturbance. These associations increased in both strength and magnitude with increasing symptom frequency, with those reporting symptoms at least 3×/week indicating the highest prevalence of depression, anxiety, and sleep disturbance, and the shortest average sleep duration.

While the cross-sectional nature of this survey study precludes determination of temporal relationships, the high RLS prevalence observed may help explain the elevated rates of both sleep disturbance and depressive disorders documented in West Virginia residents.^{28,29} The observed relationship of RLS with mood and sleep disorders may also be bidirectional. Poor sleep or mood may precipitate or exacerbate RLS via, for example, adverse effects on autonomic regulation, HPA axis function, neuroendocrine profiles, motor excitability, and pain processing.²

Direct comparisons of RLS prevalence across studies remain challenging due to broadly differing diagnostic criteria for RLS, differing definitions of clinically significant RLS, and wide variation in targeted populations.^{1,2} Nonetheless, prevalence of RLS observed in this Appalachian population was higher than that reported in prior studies of US and Western European primary care populations that used similarly stringent criteria and/or clinical confirmation to define RLS.^{1,12,33-35}

Documented prevalence of RLS in primary care settings has typically averaged higher than that reported in population cohorts or random samples from the general population, possibly reflecting overall poorer health in primary care patients.¹ Primary care patients may also be more likely to seek medical care for conditions related to RLS.^{1,39} The definition of clinically significant RLS has varied across studies, from no symptom frequency or severity requirement³⁶ to symptoms at least twice/week with at least moderate distress.^{33,40} In this study, RLS symptoms 1-2×/week were associated with significantly elevated disturbance of both sleep and mood, suggesting that RLS may be associated with substantial burden even in those with relatively low frequency of symptoms. While research assessing the potential dose-response associations of RLS severity to sleep quality and affective disorders is sparse, several previous studies have documented elevated sleep and mood disturbance in those with RLS.^{1,2,41,42}

Consistent with most, but not all previous studies,² we found RLS prevalence to be elevated in women and older adults, appearing to peak in the sixth decade. Relatively few studies have specifically examined the association of RLS to socioeconomic indices, including education, income, and employment, and even fewer have assessed the relation of RLS to race/ethnicity or marital status.^{1,43} In this investigation, participants with RLS were less likely to be college educated and more likely to be lower income, in agreement with some,^{20,21,23} but not other studies^{21,44,45} in the general population. Likewise, in agreement with a state-wide survey study of 1,803 Kentucky residents,²¹ but in contrast to findings from a second large

European study,²² we found no association between RLS and marital status. Those who were unemployed or disabled were also significantly more likely to meet RLS criteria in this population of WV primary care patients. Three studies have examined the link of RLS to unemployment,^{22,23,43} two suggesting elevated RLS prevalence^{22,43} and a third, increased risk for incident RLS²³ in unemployed adults; to our knowledge, the association of disability has not been investigated in previous studies. Our findings of reduced RLS prevalence in minority participants are in agreement with data from a previous study in two large US adult cohorts,⁴⁶ although no differences between blacks and non-Hispanic whites were reported in another study of 1,028 Baltimore adults.⁴⁷

While caffeine consumption is often cited as an exacerbating or precipitating factor for RLS,⁴⁸ evidence to date is sparse, with no studies to date documenting a significant positive association.^{22,44,49} Consistent with findings of recent population-based studies,^{44,49} we likewise found no association between RLS and caffeine consumption. In contrast to some^{20-22,24,43,50} but not other previous studies,^{44,49,51,52} RLS was not significantly related to smoking in this population after adjustment for other factors, although univariate analysis suggested a positive association. Consistent with findings from several previous investigations,^{2,17,53,54} RLS was strongly and positively associated with comorbidity in this study. Likewise, the strong, positive link between RLS and obesity observed in this study is in agreement with most, although not all previous studies.^{2,46,50,55}

Strengths and Limitations

Strengths of this survey study include the relatively large number of primary care patients in our clinic-based sample, and the high study participation rates in an Appalachian region. We used established international criteria to define RLS⁴ and questions based on a previously validated diagnostic questionnaire,³⁰ assessed symptom frequency, and asked specific questions regarding the presence of potential mimics to reduce risk of misclassification.⁵⁶ Information on symptom frequency allowed evaluation of potential dose-response associations. In addition, participants provided comprehensive self-report information on numerous potential correlates and confounders, including demographics, lifestyle characteristics, mood and sleep patterns, and health-related factors. The survey was presented as a study to examine typical sleep patterns and correlates in Morgantown area residents, with no mention of sleep deficits, mood disorders, or RLS; thus participation bias associated with either RLS or associated impairment in sleep and mood, while possible, is unlikely.

Limitations of this pilot survey are also several. Participants were restricted to primary care patients from a predominantly rural, Appalachian community, and findings may thus not be generalizable to other populations. We lacked data on certain lifestyle characteristics, including alcohol consumption, which has been associated with RLS in at least two prior investigations.^{21,22} Although we did have information on diagnosed anemia, we lacked data on blood levels of ferritin, hemoglobin levels, or other analytes potentially related to RLS. In addition, while we collected general information on medication use for health chronic conditions, including depression and anxiety, we did not collect information on specific medications (e.g.,

tricyclic antidepressants or selective serotonin uptake inhibitors) or on medication use for other serious mental health conditions (e.g., schizophrenia or psychosis) which could potentially exacerbate RLS.⁵⁶ However, the evidence regarding the association of psychotropic medication to RLS remains inconsistent. For example, while some investigators report SSRIs can precipitate RLS,⁵⁷ other studies have documented no association⁵⁸ or a reduction in RLS symptoms.⁵⁹ Moreover, excluding those on medication for depression or anxiety (which would be expected to capture most psychotropics thought to be linked to RLS⁵⁶) did not appreciably alter prevalence estimates in this population, and excluding those on medication for any chronic condition yielded only modest reductions in RLS prevalence, suggesting that medications are unlikely to account for the high rates of RLS observed in this population.

Exclusion of participants with missing data on covariates may have introduced selection bias. Unmeasured confounding might also help explain our findings, although our ability to control for a large number of both known and potential factors previously linked to RLS renders this possibility less probable. Thirteen respondents reported a diagnosis of RLS, but did not meet current symptom criteria. While some of these participants may have been misdiagnosed with RLS, others may have experienced RLS, for example, only during pregnancy or in association with since corrected anemia. One of the 13 also reported taking RLS medications, which may have led to symptom relief. Although based on questions adapted from a validated questionnaire³⁰ and incorporating questions designed to exclude common mimics, RLS determination was reliant on self-report, and some degree of diagnostic error is thus possible. However, affirmative response to all four essential criteria, coupled with the absence of discomfort due to leg cramps or positional discomfort renders misdiagnosis less likely.^{56,60} In addition, excluding from our analysis participants with specific chronic conditions linked to RLS did not appreciably alter our findings regarding either the prevalence or correlates of RLS, suggesting that these comorbid conditions are unlikely to explain the high prevalence of RLS, or the strong dose-response associations of RLS to mood and sleep impairment noted in this population. Ascertainment of medical diagnoses was based on self-report, potentially introducing bias. While our target population comprised WVU primary care patients, who are more likely to seek and receive medical care, and thus to be better informed about their health and medical conditions than a general WV population, misclassification remains possible. A validation study of a broader Appalachian population in the Ohio valley using medical records showed adequate concordance (74%) and excellent specificity (over 95%) for self-reported diabetes, and very high concordance (> 99%) for self-reported cancers (unpublished data). Nonetheless, self-report of chronic illness has been shown to be vulnerable to misclassification and especially to reduced sensitivity,⁶¹⁻⁶³ possibly biasing estimates of association towards the null. In addition, given that depression and other mental health disorders remain significantly underdiagnosed in US primary care and other populations,⁶⁴⁻⁶⁶ depression and anxiety disorders were likely under-ascertained in this study, possibly attenuating our observed associations of these conditions to RLS.

As in most other epidemiological studies of RLS, our data are cross-sectional, precluding determination of causality. Clearly,

prospective studies are needed to evaluate potential risk and causal factors underlying the development and progression of RLS, as well as the specific effects of RLS on health and well-being.

CONCLUSIONS

Findings of this preliminary anonymous survey study suggest that RLS prevalence is high in this Appalachian primary care population even when those with associated comorbidities were excluded. RLS also showed a strong, dose-response association to mood and sleep impairment, and may help explain the elevated rates of both depression and sleep deficits reported in WV residents. However, larger prospective studies are needed to investigate potential causal relationships and to enhance our still incomplete understanding regarding both the etiology and sequelae of RLS in this and other populations.

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